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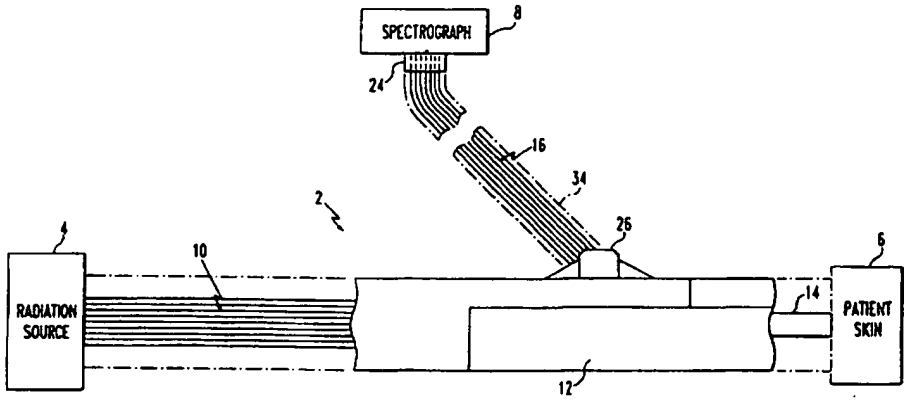
(54) Title: METHODS AND APPARATUS FOR NON-INVASIVE GLUCOSE SENSING: NON-INVASIVE PROBE



(57) Abstract

Disclosed is a probe (2) suitable for use in the non-invasive sensing of glucose concentrations in the body of a patient. The probe (2) includes at least three radiation receiving fibers (16) extending between a probe body (12) and a spectrograph (8), and spaced apart from each other in a substantially uniform manner and aligned in a predetermined fixed pattern at the probe body (12). A radiation transmitting means (10) conducts radiation from a radiation source (4) and extends from the radiation source (4) to the probe body (12). The radiation transmitting means (10) is formed in the probe (2) into a ring to conduct radiation in a ring shaped area immediately surrounding each of the receiving fibers (16). The radiation transmitting means (10) and the receiving fibers (16) terminate at the probe body (12) in a unitary structure having an outer surface configured for contacting the skin of a patient. The ring passes radiation from the radiation source (4) into the patient in the areas immediately surrounding each receiving fiber (16). The receiving fibers (16) detect the radiation passing back out of the patient and pass this detected radiation to the spectrograph (8).

METHODS AND APPARATUS FOR NON-INVASIVE GLUCOSE SENSING: NON-INVASIVE PROBE

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to the non-invasive sensing of blood glucose levels and, more particularly, to a non-invasive probe suitable for use with a non-invasive blood glucose monitor for patients with diabetes.

2. Description of the Prior Art

It is generally known in the art that radiation, particularly near-infrared radiation over a range of wavelengths, can be projected in a non-invasive manner on a portion of the body of a patient. The resulting radiation emitted from that portion of the body, either scattered or transmitted after absorption and scattering, can be detected and processed to derive an expression of the detected radiation as a function of wavelength and, therefrom, the concentration of blood glucose. Since the detected radiation is a continuous signal covering all of the wavelengths in the range of interest, it is necessary for further analysis to separate the intensities of radiation at the various individual wavelengths, or smaller bands of wavelengths, to extract the desired blood glucose level information.

U.S. Patent Nos. 5,070,874 and 5,460,177 describe methods for the non-invasive measurement of blood glucose levels. In general, these methods use a spectrophotometer to measure the absorbance of the near-infrared radiation at different wavelengths across the range of interest. The absorbance plotted against the wavelengths constitutes a spectrum. By analyzing the spectrum, the blood glucose levels, or changes thereto, can be determined. As the blood glucose levels vary, the detected spectrum changes slightly.

In order to make the measurements discussed above, the radiation must be transmitted from a radiation source to the skin of a patient and the detected radiation received back from the patient must be collected and carried to the spectrophotometer for further analysis.

invention is designed to operate in intimate contact with its intended target, i.e., the human skin, and deliberately avoids direct surface reflections. In a preferred embodiment, the probe combines an incoherent transmissive fiber optic bundle with a small number of spaced receiving fibers arranged in a specialized, regular pattern to optimize received-signal intensity in a glucose measurement application. A preferred embodiment also includes uniquely designed features to thermally and/or mechanically isolate the receiving fibers extending from the probe in order to enhance their operation in a glucose measurement application.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a schematic view of the elements of a probe in accordance with the present invention;

FIG. 2 is an end view of the transmitting fiber bundle extending from the radiation source;

FIG. 3 is an end view of the transmitting fiber bundle and receiving fibers where they contact the skin of a patient;

FIG. 4 is an end view of the receiving fibers where they enter the spectrograph; and

FIG. 5 is a schematic view showing one embodiment of an arrangement for protecting the receiving fibers between the patient contact and the spectrograph.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

A probe 2 suitable for use in the non-invasive sensing of glucose concentrations in the body of a patient in accordance with the present invention is shown in FIGS. 1-5. As shown in more detail in FIG. 1, the present invention includes a bifurcated fiber optic bundle capable of transmitting radiation, particularly in the near-infrared range, and the fiber optic bundle has terminations at a radiation source 4, at the patient skin 6 and at a spectrograph 8. These terminations are shown in more detail in FIGS. 2, 3 and 4, respectively, and will be discussed hereinafter in more detail. With continued

wavelength range of the radiation generated by the radiation source 4.

As shown with reference to both FIGS. 1 and 3, the transmitting fibers 10 and the receiving fibers 16 join in the probe body 12, and the entire assembly is splayed out in a quasi-rectangular pattern at the contact section 14 or skin termination, where all fibers 10, 16 are connected in a unitary structure, such as by epoxy 17 or other adhesive, and preferably terminate in a common plane achieved by polishing or other means forming an outer surface configured for contacting the patient skin 6. Although a flat contact is presently preferred, other arrangements are possible. In a preferred embodiment, the fibers 10, 16 are arranged in seven hexagonally packed rows. Shown in FIG. 3 is a preferred embodiment including eleven receiving fibers 16a through 16k constrained to a central row, and each receiving fiber 16 is completely surrounded by transmitting fibers 10. In this arrangement, three transmitting fibers 10 in the central row are provided immediately on each side of each receiving fiber. All other rows shown in FIG. 3 contain only transmitting fibers. Therefore, it can be seen that each receiving fiber is at the center of three concentric hexagons or rings of transmitting fibers 10. For example, a first ring of transmitting fibers 10 surrounding receiving fiber 16a includes six transmitting fibers 10a. The twelve transmitting fibers 10b immediately contacting transmitting fibers 10a form a second ring surrounding receiving fiber 16a. The eighteen transmitting fibers 10c immediately contacting transmitting fibers 10b form a third ring surrounding receiving fiber 16a. Similar rings are formed around each of the ten other receiving fibers 16. It can be seen that certain transmitting fibers 10 form part of a ring around adjacent of the receiving fibers 16. For example, transmitting fiber 10a in the central row of fibers and immediately to the right of receiving fiber 16a as viewed in FIG. 3 is part of the first ring surrounding

before it returns through the patient skin 6 and into the receiving fibers 16. This selective absorption varies with the glucose level of the patient. Thus, the spectral pattern of the received power contains the information needed to make the glucose level measurement, which is the overall goal of the monitor with which the probe 2 of the present invention is used.

The isolation between the transmitting fibers 10 and the receiving fibers 16 is an important feature of this invention, since the isolation significantly improves the received spectral information's signal-to-background ratio, thereby permitting the subtle glucose information to be readily extracted. Similarly, surrounding each receiving fiber 16 by the chosen number of transmitting fibers 10 at the patient skin 6 optimizes the glucose absorption information content in the received signal, by providing a statistically appropriate average penetration path of optical power within the patient skin 6.

The receiving fibers 16 transfer the information-carrying infrared energy to the spectrograph 8, where it is optically dispersed for analysis. At the spectrograph 8, the receiving fibers 16 are arranged in a pattern compatible with the size and shape of each picture element or pixel at the output of the spectrograph 8. In one embodiment of a spectrograph 8, the pattern of the output pixels is linear, with matching rectangular sensor pixels. For example, the spectrograph 8 can be designed so that a grating therein disperses a collimated beam from a source mirror into a multiplicity of wavelengths, each diffracted in a slightly different direction. This process forms multiple overlapping collimated beams, each corresponding to a specific wavelength and direction, all of which are aimed substantially at a camera mirror in the spectrograph 8. The camera mirror focuses each of the various wavelengths at a slightly different location, forming an extended continuum of overlapping source array images at the detector array location.

numerical aperture of the receiving fibers 16 and the optics of the spectrograph 8 must be compatible, and the receiving fibers 16 and transmitting fibers 10 must be transmissive throughout the spectral region of operation. In some embodiments, these requirements necessitate transmission at wavelengths near or beyond 2 μm. In such cases, fibers made substantially of fused silica are preferred. Low-OH^- fiber is also preferred because absorption by that radical may be confused with glucose absorption in certain spectral regions, notably within the desired near-infrared range, and particularly in view of the inherently low level of glucose signals compared to the general level of skin signals.

In the preferred embodiment, hard-clad, low-OH^- optical fiber of approximately 0.39 numerical aperture (n.a.) and 0.230 mm diameter (0.200 mm core) is used as the transmitting fibers 10 and the receiving fibers 16. The numerical aperture of the fiber is deliberately chosen to be larger than that of the spectrograph 8 (~0.3 n.a.) to ensure that the optics and grating are overfilled, even in the presence of operational vibration and thermal effects. One such fiber is 3M's FT-200-LMT, but other similar low-OH^- fibers and other combinations of diameter and n.a. compatible with spectrographs or sensors of the preferred embodiment or other types are included within the scope and spirit of this invention.

In order to reduce the effects of vibration and thermal changes, the receiving fibers 16 are, in a preferred embodiment, enclosed in an insulating material type of structure. This is shown in more detail in FIG. 5. Although encasing the receiving fibers 16 in insulating material would appear to be straightforward, an approach which merely provides a thick insulating material wrapping around the receiving fibers 16 will tend to make the overall structure less flexible. In the present invention, this problem is overcome by two unique methods. The first

tube 34 does not damage or stress the receiving fibers 16. The slip fit arrangement discussed above with slip ring 36 could be provided at the receiving fiber housing 38 adjacent the spectrograph 8, although the arrangement shown in FIG. 5 is believed to be preferred. It is preferred that the receiving fiber housing 38 be filled, such as through hole 40, with an insulating material 42 and that the interior of the inner tube 32 be filled with an insulating material. The first enclosure 26, the interior of the inner tube 32 and the receiving fiber housing 38 can be filled simultaneously with the same material through hole 28 or, preferably, through hole 40, since these elements are all interconnected in their interiors.

In a preferred embodiment, the receiving fibers 16 are surrounded by the inner tube 32 which is an insulating multi-layer sheath that encapsulates the receiving fibers 16. The receiving fibers 16 are loosely enclosed over their full length inside the lumen of a typically medium durometer elastomeric inner tube that exhibits adequate insulating properties. For optimal thermal and mechanical isolation, the receiving fibers 16 inside the lumen of the inner tube 32 may then be further protected by backfilling the inner tube 32 with a low durometer, insulating elastomeric potting compound 44. This material, inserted in a fluid state and then cured, surrounds the receiving fibers 16 directly and provides both additional thermal isolation and mechanical vibrational dampening to reduce microbending effects. Over the inner tube 32 in which the receiving fibers 16 are potted is an outer tube 34 of adequate insulating properties which provides additional thermal and mechanical isolation. The outer tube 34 may be a typically medium durometer elastomeric tube or may be a more rigid tube. Multiple layers of various insulating materials may also be used to achieve the same effects as described above.

The foregoing discussion and the attached drawings are illustrative and non-limiting. They are

We claim:

1. A probe suitable for use in the non-invasive sensing of glucose concentrations in the body of a patient, said probe comprising: at least three radiation receiving fibers extending between a probe body and a spectrograph, and spaced apart from each other in a substantially uniform manner and aligned in a predetermined fixed pattern at said probe body, a radiation transmitting means for conducting radiation from a radiation source and extending from the radiation source to the probe body, with said radiation transmitting means formed in said probe into ring means for conducting radiation in a ring-shaped area immediately surrounding each of said receiving fibers, with said radiation transmitting means and said receiving fibers terminating at said probe body in a unitary structure having an outer surface configured for contacting the skin of a patient, wherein the ring means passes radiation from said radiation source and into the patient in the areas immediately surrounding each receiving fiber and the receiving fibers detect said radiation passing back out of the patient and pass said detected radiation to the spectrograph.

2. The probe of claim 1 wherein said radiation transmitting means is formed of a plurality of radiation transmitting fibers and the ring means is formed from certain of said transmitting fibers immediately surrounding each receiving fiber in a ring-shaped pattern at the outer surface.

3. The probe of claim 2 wherein each receiving fiber is separated from its immediately adjacent receiving fiber by at least one transmitting fiber.

11. The probe of claim 1 wherein the receiving fibers are covered by an enclosure in the area between an outer portion of the probe body and their termination at the spectrograph.

12. The probe of claim 11 wherein the enclosure includes a first insulating enclosure immediately adjacent the probe body and a second insulating enclosure extending along the remaining length of the receiving fibers.

13. The probe of claim 12 wherein the first insulating enclosure is a hollow structure filled with an insulating material.

14. The probe of claim 12 wherein the second enclosure includes a first insulating tube immediately surrounding the receiving fibers and a second insulating tube spaced from and surrounding the first insulating tube.

15. The probe of claim 14 wherein one end of the second insulating tube is securely attached to the first insulating tube, while the other end of the second insulating tube is loosely attached to the first insulating tube and is moveable with respect thereto.

16. The probe of claim 15 wherein the end of the first insulating tube adjacent the probe body is attached to a slip ring which is attached to the first enclosure and the end of the second insulating tube adjacent the probe body is slip fit onto the slip ring.

17. The probe of claim 16 wherein the ends of the receiving fibers opposite the probe body are securely attached to a receiving fiber housing and the first insulating tube and second insulating tube are each securely attached to the receiving fiber housing.

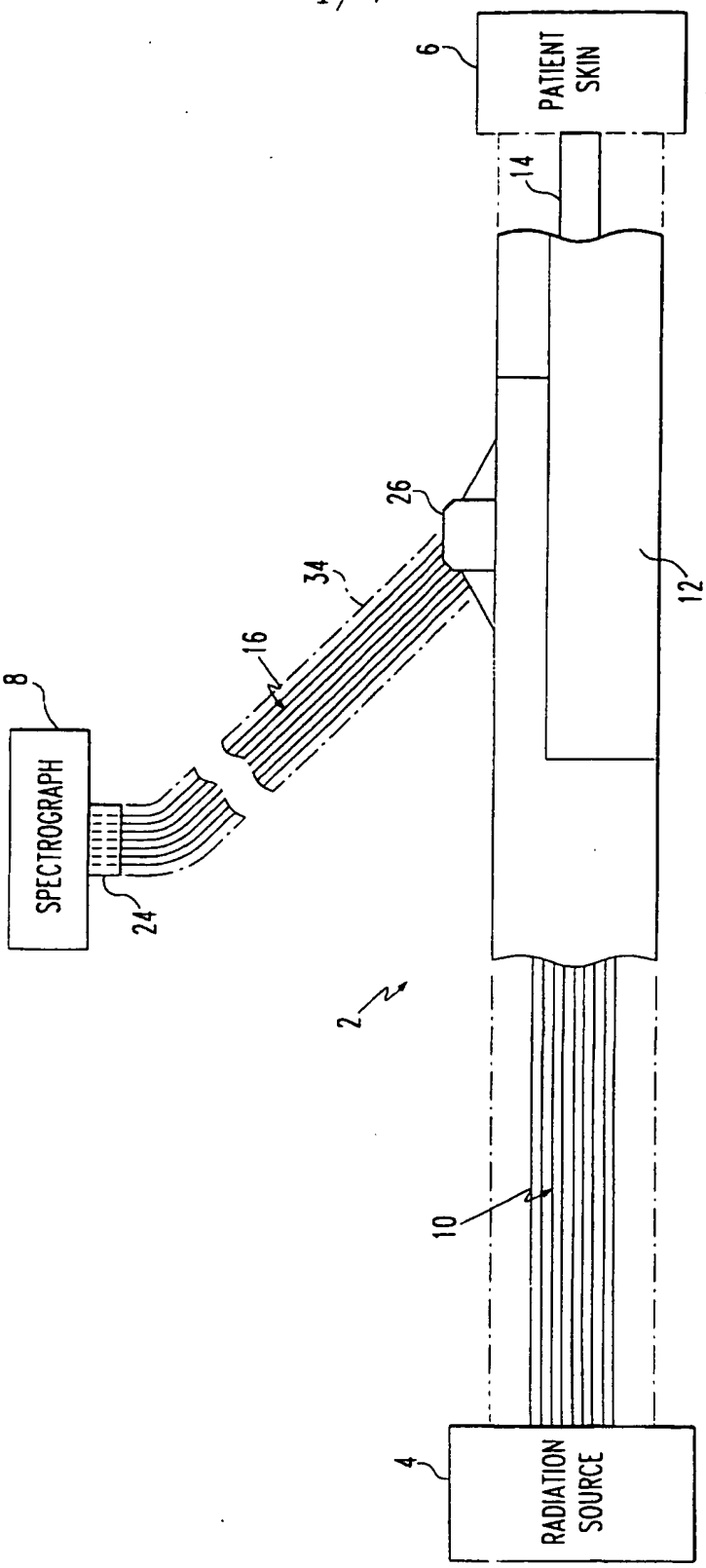

6
PATIENT SKIN
14
26
34
16
8
SPECTROGRAPH
24
12
2
10
4
RADIATION SOURCE

FIG. 1

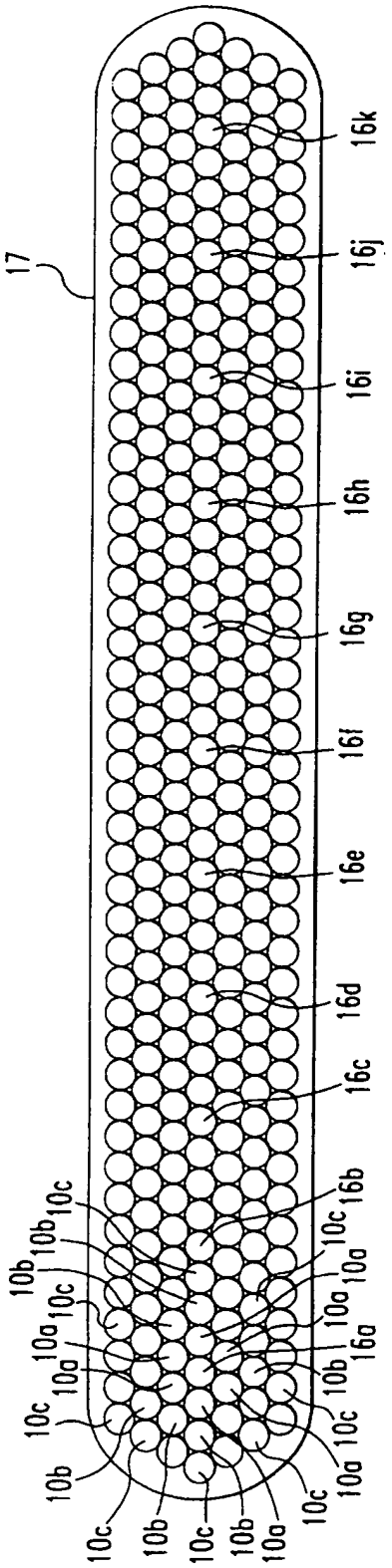


FIG. 3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/01450

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61B 5/00
US CL :128/633

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 128/633, 664, 665; 356/39; 385/115

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,070,874 A (BARNES et al) 10 December 1991, col. 5, line 49 to col. 6, line 68.	1-20
A	US 5,178,142 A (HARJUNMAA et al) 12 January 1993, col. 5, line 26 to col. 7, line 24.	1-20
A	US 5,419,321 A (EVANS) 30 May 1995, col. 5, line 19 to col. 6, line 23.	1-20
A, P	US 5,596,992 A (HAALAND et al) 28 January 1997, entire document.	1-20

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
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